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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,803	03/31/2008	Peter John Coles	PB60432	4407

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GlaxoSmithKline
GLOBAL PATENTS -US, UW2220
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EXAMINER	
AL-AWADI, DANAH J	

ART UNIT	PAPER NUMBER
1615	

NOTIFICATION DATE	DELIVERY MODE
08/19/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

US_cipkop@gsk.com

Office Action Summary	Application No.	Applicant(s)	
	10/567,803	COLES ET AL.	
	Examiner	Art Unit	
	DANAH AL-AWADI	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-14 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-14 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1 page 06/09/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of Applicant's amendments and remarks filed 06/09/2010. The Examiner acknowledges the following:

Claims 10, 11 have been amended.

Claim 15 is cancelled.

Claims 1—14 and 16 currently represent all pending claims under examination.

INFORMATION DISCLOSURE STATEMENT

Information Disclosure Statement (IDS) filed 06/09/2010 is acknowledged.

WITHDRAWN REJECTIONS

Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

NEW REJECTIONS

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 10-14 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is not clear what applicant intends by the limitation of claim 10 "a compound." This is very vague and can encompass a multitude of things. Page 4 lines 33- page 5 line 10 of the specification, states in the broadest aspect of the present invention an oral dosage form comprising an erodible core, which core comprises Compound A (Rosiglitazone) or a pharmaceutically acceptable salt or solvate thereof and an anti-diabetic. There is no mention of inclusion of more than just another anti-diabetic agent. In other words there are not multiple anti-diabetic agents mentioned to be included. Page 11, lines 7-20 of the specification teaches delayed release of at least one of Compound A (Rosiglitazone) or a pharmaceutically acceptable salt or solvate thereof and another antidiabetic agent. There is no mention of including compound A (Rosiglitazone), with Metformin and another anti-diabetic compound. There is no mention of the inclusion of two antidiabetic agents with the Rosiglitazone. The examples are further directed to the inclusion of two anti-diabetic compounds (e.g. Rosiglitazone and Metformin). Furthermore, there is nothing in the specification that states what this other compound might be. It could encompass any known compound. Applicants have not pointed to where in the specification there is support for this additional component should it be intended to be another anti-diabetic. Therefore, the examiner is interpreting the new limitation of "a compound" to encompass any compound which would read on having excipients. Claims 11-14 and 16 are rejected due to their dependency from claim 10 with the new limitation "a compound".

MAINTAINED REJECTIONS

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 10-14, and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Martini et al. WO 03/068195 and Lewis et al. US 2004/0081697.

With regards to pending claims 10, 15, and 16, Martini et al. WO 03/068195 (hereafter the '195 publication) teaches an oral dosage tablet form comprising an erodable core which comprises 5-[4-[2-(N-methyl-N-(2 pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione (Rosiglitazone) (abstract, page 3 lines 25-36, page 4, lines 1-4, page 6 lines 15-37, page 7, page 8 lines 20-26 and lines 34-36). The '195 publication teaches an erodable coating around the core, that comprises one or more openings leading to the core wherein the coating is erodable under predetermined pH conditions. With regards to the limitation that the coating is erodible in the pH range from 4.5 to 8, the '195 publication teaches that the coating can erode at a pH greater than 4.5 (line 5 page 7).

The '195 publication does not teach the inclusion of Rosiglitazone with another antidiabetic agent which is Metformin, however Lewis et al. US 2004/0081697 (hereafter the '697 publication teaches an oral dosage form comprising an erodable core which comprises Rosiglitazone and another antidiabetic agent which is Metformin (paragraphs [0072], [0073], [0017], [0018], [0027], (Example 1-3), claims 1, 2, 11, and 15).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to formulate a erodable core that comprises the compounds, Rosiglitazone and another antidiabetic agent which is Metformin. One would have been motivated to do so because the '697 publication teaches that certain modified release pharmaceutical compositions allow administration of a single daily dose of Rosiglitazone and antidiabetic such as Metformin, to provide an advantageous delivery of drug for maintaining effective glycemic control with no adverse side affects for the treatment of diabetes mellitus.

With regards to pending claim 11, the '195 publication teaches a coating that comprises one or more openings extending substantially completely through the coating but no substantially penetrating the core and communicating from the environment of use to the core and wherein release of the compound from the core occurs substantially through the openings and through erosion of the coating under pre-determined pH conditions.

With regards to pending claims 12 and 13, the '195 publication teaches that the coating is enteric and that it is non-permeable.

With regards to pending claim 14, the '195 publication teaches that the core can provide for immediate release of the compound via the openings. The '195 publication does not teach the immediate release of Rosiglitazone and the antidiabetic agent Metformin, however the '195 publication does mention that by adjusting the variables and surface area of the core, the release rates in the different environmental conditions can be harmonized to obtain comparable release rates under different body conditions. As discussed supra it would have been prima facie obvious to one of ordinary skill in the art to formulate a tablet that includes Rosiglitazone and an antidiabetic agent such as Metformin. Furthermore, the '697 publication teaches the use of eroding matrices provides for sustained release of each of the active agents.

RESPONSE TO ARGUMENTS

Applicant's arguments with regard to the rejection of claims 1-14, and 16 (noting claim 15 is now cancelled) under 35 U.S.C.103(a) over Martini et al. WO 03/068195 and Lewis et al. US 2004/0081697, has been fully considered, but they are not persuasive.

Applicant alleges that the Examiner is using hindsight reasoning to pick and choose among the various compositions, active ingredients and dosage form elements described in the '195 publication and the '697 publication to support the 35 USC § 103 rejection.

In response, the Examiner respectfully submits that it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Applicants further argue that the claimed oral dosage form comprises more than just an erodible core containing Rosiglitazone and Metformin. In other words, applicant agues that there are additional compounds added.

In response, the examiner respectfully submits that, the specification does not support having an additional compound included with Rosiglitazone and Metformin if it were intended to be another anti-diabetic. However, assuming that this additional compound is intended to be another anti-diabetic agent, one would have been motivated to include another anti-diabetic agent since it is known to be effective for treating diabetes, "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (see MPEP 2144.06).

Furthermore, it is not clear what this additional compound can be. Therefore, water could theoretically meet this limitation. The '697 publication teaches the core comprises active agent or agents. Additionally, the '697 publication teaches additional excipients can be included such diluents, binders, lubricants, surfactants, etc.. The '697 publication teaches the core consists of magnesium stearate (i.e. a compound).

Applicants further argue that the '195 publication discloses a oral dosage formulation designed for delivery of a pharmaceutically active weak base defined as a base with the conjugate acid of which has a pKa of less than 11.5. Metformin posses a pKa of 12.4, and therefore the '195 publication does not have motivation as being suitable or desirable for delivery of a pharmaceutically active base, the conjugate acid which has a pKa of greater than 11.5.

In response, the examiner respectfully submits that there is no suggestion in the prior art references that the composition does not allow for inclusion for any other components. It would have been obvious to the skilled artisan to try to put in one formulation to achieve the same results (i.e. treatment of diabetes). The prior art does not exclude additional components.

Furthermore, applicants argue that dosage forms containing a therapeutic amount of both Rosiglitazone and Metformin would contain amounts of Metformin that are over 100x greater than the amount of Rosiglitazone.

In response, the examiner respectfully submits that the instant claims do not recite suitable dosage amounts. It is well known and recognized in the art as evidenced by the abstract of "Rosiglitazone does not Alter the Pharmacokinetics of Metformin" (see PTO-892) that

Rosiglitazone and Metformin can be used in combination to optimize glycemic control. Co-administration of these drugs is known in the art.

The '195 publication teaches all the same structures as claimed by applicants. Applicants are including the addition of another anti-diabetic agent, specifically Metformin, however it is well known in the art that these two drugs are used in combination to optimize glycemic control, and therefore it would have been obvious to the skilled artisan to also try to include Metformin in the dosage form taught by the '195 publication.

CONCLUSION

All claims have been rejected; no claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

CORRESPONDENCE

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Danah Al-Awadi whose telephone number is (571) 270-7668.

The examiner can normally be reached on 9:00 am - 6:00 pm; M-F (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on (571) 272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/DA/
Examiner, Art Unit 1615

/Humera N. Sheikh/
Primary Examiner, Art Unit 1615